II. REMARKS\ARGUMENTS

A. Regarding the Amendments

Claims 2, 9, 21, and 30 are cancelled by the present amendment. Claims 1, 2-8, 10-20, 22-29, and 31 are pending in the application. Claims 1, 10, 12, 14, 15, 24, 26, and 29 have been amended.

Claims 1, 14, 26, and 29 were amended to specify that the urea cycle effector is limited to the group consisting of arginine, ornithine, citrulline, and mixtures thereof. Support for this claim is found in original claim 2, at page 6, lines 28-31 of the specification, and in the tables on pages 8 and 10 of the specification.

Claims 1, 10, 12, 14, 24, 26, and 29 were amended to include solvents and excipients. Support for this amendment is found in original claim 9 and on page 11, line 15 through page 13, line 22 of the specification.

Claims 1, 14, 26, and 29 were amended to clarify that the presently claimed methods and compositions are for treating fatigue and weakness in a patient undergoing cancer chemotherapy. Support for this amendment is at page 4, lines 21-24 of the specification.

B. Rejections under 35 U.S.C. § 103

The Examiner has maintained his rejection of claims 1-31 under 35 U.S.C. § 103(a) as being unpatentable over U.S. Patent No. 5,719,134, issued to Schmidl et al. (the Schmidl reference). Specifically, the Examiner alleges that Schmidl teaches a dietary composition useful for providing nutrition to individuals with diseases and who are unable to consume food orally. The Examiner alleges that the instant claims are directed to methods and compositions for

treating or reducing the effects of malnutrition associated with a condition or disease and that it would have been obvious to use the nutritional composition of Schmidl to treat such effects.

The Examiner has also maintained his rejection of claims 1-31 under 35 U.S.C. § 103(a) as being unpatentable over U.S. Patent No. 5,550,146, issued to Acosta et al. (the Acosta reference). Specifically, the Examiner alleges that Acosta discloses a nutritional composition containing vitamins and amino acids for the treatment of various metabolic diseases. The Examiner alleges that the instant claims are pharmaceutical claims with an intended use of treating or reducing the effects of malnutrition associated with a condition or disease and that it would have been obvious to utilize the nutritional compositions of Acosta to treat metabolic disorders caused by a variety of diseases or conditions, such as cancer.

Applicant respectfully traverses both rejections because the compositions disclosed in the cited references are different than the compositions that are presently claimed. The Schmidl reference and the Acosta reference are both directed to nutritional compositions containing a broad spectrum of amino acids and vitamins. The preferred composition of Schmidl comprises 58 components, including 17 amino acids. *See* Schmidl, col. 5. Likewise, the amino acid formulations of Acosta comprise 20 amino acids. *See* Acosta, col. 21, Table 3. In contrast, the compositions of the present invention consist of riboflavin; an effector of the urea cycle selected from the group consisting of arginine, ornithine citrulline, and mixtures thereof; six amino acids (alanine, glycine, serine, taurine, threonine and valine); and a suitable solvent, diluent, excipient or carrier.

The cited references do not teach or suggest the presently claimed compositions.

The instant claims use the transition phrase "consisting of" in relation to the claimed compositions. The transition phrase "consisting of" excludes any element, step, or ingredient not

specified in the claim. *In re Gray*, 53 F.2d 520, (C.C.P.A. 1931). Neither of the cited references teach nor provide motivation for compositions that are limited to the presently specified components.

The Examiner alleges that it would have been obvious to utilize the instantly claimed compositions in view of the fact that Schmidl teaches a "most preferred composition," which contains L-alanine, glycine, L-serine, taurine, L-threonine, and L-valine, L-arginine and riboflavin. As pointed out above, the most preferred composition of Schmidl contains many other components in addition to the ones listed by the Examiner. The closed "consisting of" language of the instant claims excludes these additional components. Shcmidl provides no guidance or motivation to select the presently claimed compositions from among the large number of components disclosed. Schmidl does not suggest that the presently claimed compositions would be effective for treating fatigue and weakness associated with cancer chemotherapy. In fact, cancer chemotherapy is not mentioned anywhere in the Schmidl reference.

The Examiner points out that Acosta discloses a nutritional product comprising L-alanine, L-serine, glycine, L-thrionine, L-valine, taurine, riboflavin, and L-arginine. The Examiner alleges that because Acosta teaches using such compositions to treat metabolic disorders, one of skill in the art would be motivated to supply these compositions to patients undergoing cancer chemotherapy. However, the Examiner is failing to consider that the compositions of Acosta also contain many components in addition to those listed by the Examiner (refer to Tables 1 and 3 of Acosta). These additional components are excluded by the instant claims. Acosta contains no motivation to limit the composition to the components

instantly claimed. Acosta contains no suggestion that such limited compositions would be effective for treating fatigue and weakness associated with cancer chemotherapy.

The motivation to use the limited compositions of the present invention derives from the fact that total parenteral nutrition (TPN) is presently not a desirable treatment for fatigue and weakness in cancer patients because TPN has been shown to facilitate cancer progression by supplying large quantities of nutrients necessary for cancer growth. *See* page 3, lines 4-19 of the instant specification. In contrast to TPN, the presently claimed compositions and methods utilize selected amino acids and riboflavin (vitamin B-2), which reduce the toxic effect of chemotherapy and at the same time have a slight inhibitory effect on cancer. The presently claimed compositions are effective at treating fatigue and weakness in patients undergoing cancer chemotherapy. *Refer to* Examples described in the instant specification. The cited references do not teach or suggest the presently claimed compositions and they give no suggestion that the presently claimed compositions would be beneficial to patients undergoing cancer chemotherapy.

The Examiner alleges that one of skill in the art would be motivated to provide the compositions of Schmidl and Acosta to patients undergoing cancer chemotherapy. Even if one did so, they still would not be practicing the claimed invention because the compositions of Schmidl/Acosta are different than those of the present claims. The compositions of Schmidl/Acosta contain many components that are excluded by the consisting of language of the present claims. Further, Schmidl/Acosta do not provide any motivation for selecting the presently claimed compositions.

The Examiner states that the selection of a known material based on its suitability for its intended use supports a prima facie obviousness determination (*citing* Sinclair & Carroll Co. v.

Interchemical Corp., 325 U.S. 327 (1945). Applicant whole-heartedly agrees, but the present claims are not directed to known materials selected for their intended use. The presently selected materials are compositions consisting of a very specific and closed list of components. The art cited by the Examiner provides no guidance as to how to select these components from the many components contained therein so as to avoid the problems associated with TPN described in the specification. The fact that the presently claimed combinations of components are suitable for the intended purpose of alleviating fatigue and weakness associated with cancer chemotherapy is apparent only from the present disclosure, not from the art cited by the Examiner.

The Examiner points out that claims 1 and 26 recite the word "comprising," which is open claim language. Applicant points out that while claims 1 and 26 are open with respect to the method of alleviating fatigue and weakness in a patient undergoing cancer chemotherapy, the claims are closed with respect to the recited compositions. When the phrase "consists of" appears in a clause of the body of a claim, rather than immediately following the preamble, it limits the elements set forth in that clause. *Mannesmann Demag Corp. v. Engineered Metal Products Co.*, 793 F.2d 1279 (Fed. Cir. 1986). The phrase "a composition consisting of" therefore limits the components of the composition to those components set forth in the claims.

The Board of Patent Appeals and Interferences addressed this issue in *Ex Parte Lata Ramanthan, et al.*, Appeal No. 1997-0711, 2002 WL 851826 (Bd. Pat. App. & Interf.), when they considered the following claim:

> 11. A method for producing antibodies which specifically bind to and inhibit the binding of human Interleukin-4 (IL-4) to receptors *comprising* administering to an animal a sufficient quantity of a polypeptide *consisting of* amino acid residues 61 to 82 of IL-4, wherein the animal produces antibodies against the polypeptide, said antibodies being able to specifically bind to human IL-4 and are able to inhibit the binding of human IL-4 to cellular receptors.

(emphasis added). The Board interpreted claim 11 as being open to the administration of other ingredients in addition to the recited polypeptiede, but found that the polypeptide is limited to only the specified amino acids recited in the claim. The board found the claim patentable over prior art that taught the polypeptide conjugated with a carrier (i.e., the polypeptide including other amino acids). The board stated that the prior art failed to specifically disclose or suggest that the uncoupled polypeptide could be used for the claimed purpose.

With the Board's decision in *Ex Parte Lata Ramanthan, et al.* as a guide, one would construe claims 1 and 26 of the instant application as being open with respect to a method of alleviating fatigue and weakness in a patient undergoing cancer chemotherapy, but being closed with respect to the cited compositions. In other words, the method can include steps in addition to providing the claimed compositions. Such steps might include massage, aromatherapy, or even the administering of other agents such as painkillers or tranquilizers to a patient. However, the method is closed with respect to the recited compositions. If the method does not include administering a composition consisting of the recited components, and only the recited components, then that method falls outside of the claim. The Schmild/Acosta references do not teach administering such a composition and therefore do not render these claims obvious.

Applicant respectfully requests that the rejections over the Schmidl and Acosta references be withdrawn, for the reasons described above.

C. Indefiniteness

The Examiner indicated in a telephone conference that the terms "toxic, nutritional and metabolic disturbances associated with cancer and cancer chemotherapy" rendered claims 1, 14, 26, and 29 indefinite. Thought these claims are not presently rejected under 35 U.S.C. § 112,

Applicant has amended them to clarify that the claims are directed to specific methods and compositions for treating fatigue and weakness in a patient undergoing cancer chemotherapy.

D. Information Disclosure Statement

The Examiner requested that the Koretz reference be submitted on a PTO Form 1449. This reference was submitted on a PTO Form 1449 with the Information disclosure Statement that was filed Feb. 7, 2002. This reference is designated C5.

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The Examiner is invited to contact the undersigned patent agent with any questions, comments or suggestions relating to the referenced patent application.

Respectfully submitted,

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